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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,829	03/29/2004	Alan D. King	04-100	9996

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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,829	KING ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26,28-31,37,38,40,42,44,47-50 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,26,28-31,37,38,40,42,44,47-50 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and Declaration under Rule 1.131 filed August 19, 2005, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 25, 26, 28-31, 37, 38, 40, 42, 44, 47-50, and 52 are pending and are presented for examination.

Claim Rejections - 35 USC § 112

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 is indefinite since it comprises the recitations, "said macromolecules" and "said organ treating agent", which lack antecedent basis. Parent claim 25 does not recite "macromolecules" or an "organ treating agent". Thus, claim 47 is rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 102

Claims 25, 26, 29-30, 37, 47, 49, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Gross et al. (US Pat. 5,356,632).

Gross et al. discloses a transdermal drug delivery device comprising an anode electrode and a cathode electrode each coated with a gel containing a drug (column 3, lines 9-18). A gel is considered both a solid and a liquid (http://en.wikipedia.org/wiki/Gel). Different configurations

of the drug delivery device are provided, including a configuration as shown in Figure 6. This configuration comprises multiple electrodes in parallel rows (column 4, line 58 through column 5, line 27). Furthermore, the drugs that may be delivered include beta-blockers and analgesics (column 3, lines 46-49).

Claims 49 and 50 are product-by-process claims. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of

the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Applicant's arguments filed August 19, 2005 have been fully considered but they are not persuasive. First, Applicant notes that Applicant's currently claimed invention does not require a gel or liquid as are required by Gross et al. However, as written, the claims do not exclude the use of liquid or gel coatings. Further still, claim 30 recites that the molecules in the static layer are in a gel.

Additionally, Applicant argues that the Gross patent, which Applicant notes uses electrophoresis to move material away from the liquid containing gel, does not use applied electric fields for electroporation to get material into cells after they are released from the electrode. However, since an electric current is used in the Gross patent, an electric field is applied to the releasable molecules on the Gross electrode. Moreover, electrophoresis is defined as "the movement of an electrically charge body under the influence of an electric field" (http://en.wikipedia.org/wiki/Electrophoresis). It is respectfully submitted that Gross et al. clearly meets the claim requirement that the "releasable molecules to be delivered into biological cells in the penetrated tissues by an applied electric field" since an electric field is applied to the releasable molecules on the electrode which allows for the molecules to be released for delivery

into biological cells in the tissues. The instant claims as written do not require that electroporation is used to get material into cells after they are released from the electrode, as asserted by the Applicants. Even if the claims were written with this requirement, Gross et al. does not suggest that electroporation of the biological cells does not occur following release of molecules from the electrode.

In response to applicant's argument that Gross et al. is just for use on the surface of the skin with transdermal action, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Applicant asserts that given that Gross et al. teaches that the mere contact of the skin with the electrodes is to be avoided, Gross et al. teaches away from any electrode "penetration into tissues" and from "releasable molecules to be delivered into biological cells in the penetrated tissues". However, it is respectfully pointed out that the Gross electrode(s) are covered with a gel which prevents direct contact of the skin with the electrodes, thus implantation of the Gross electrodes still prevents contact of tissues with the electrodes. Moreover, the Applicant's currently claimed invention also is not in contact with the "penetrated tissues" since the electrode is coated with a static layer of releasable molecules. Therefore, nothing in the Gross patent, including the requirement that the electrodes not be in contact with the skin, prevents implantation of the Gross electrodes into the skin. Thus, the prior art electrodes are capable of performing the intended use of penetrating into tissues, such as skin.

It is therefore respectfully submitted that the rejection set forth herein is required.

Claim 42 is rejected under 35 U.S.C. 102(e) as being anticipated by Wang (US Pat. 6,514,762).

Wang discloses a device comprising two electrodes coated by nucleotides (column 2, lines 38-40) such as DNA and RNA (column 2, lines 65-67). The device allows for the delivery of nucleotides for "use in gene therapy for treatment or prevention of disease" (column 4, lines 16-19). Thus, Wang provides a method for DNA or RNA vaccine delivery, as a vaccine is used for disease prevention. In particular, the nucleotides may be used for treatment of cancer (column 8, lines 5-7).

Applicant's arguments have been fully considered but they are not persuasive. While claims 25, 26, 28, 29, 31, 37, 38, 40, 44, 47-50, and 52 of the instant application have an effective filing date of January 28, 1999, claims 30 and 42 do not as they cannot claim the benefit of Provisional Application 60/117,755. The disclosure of the prior-filed application, 60/117,755, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for claims 30 and 42 of this application.

With respect to the argument that unlike Wang, the Applicant's claimed invention does not require time release of nucleotides and instead, the electrode delivers a pre-measured dose, it is respectfully pointed out that claim 42 and its parent claims 25 and 37 do not recite the requirement of the delivery of a pre-measured dose. Thus, a holding of anticipation is required.

Claim Rejections - 35 USC § 103

Claims 25, 26, 28-30, 37, 47, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Hofmann (US Pat. 6,009,347).

As discussed above, Gross et al. anticipates claims 25, 26, 29-30, 37, 47, 49, and 50. However, Gross et al. does not expressly disclose needle electrodes for drug delivery.

Hofmann discusses electroporation for use in introducing foreign material into living cells (column 1, lines 9-14 and lines 34-40). Specifically, Hofmann discloses using needle electrodes (column 4, lines 33-35) and notes that "the applicant has found through experimentation that pulsing between multiple pairs of electrodes in a multiple electrode array, preferably set up in rectangular or square patterns, provides improved results over that of pulsing between a pair of electrodes" (column 4, lines 49-53). The electroporation device may comprise of an array of needles as electrodes (column 4, lines 53-61).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use needle electrodes in the Gross drug delivery device. One of ordinary skill in the art would have been motivated to do this because Hofmann indicates that needle-shaped electrodes allow for access to more deeply located cells (column 1, lines 44-45). A holding of obviousness is clearly required.

Applicant's arguments have been fully considered but they are not persuasive. Applicants notes that Hoffman teaches electrodes which do not have a coating having at least one static layer of releasable molecules to be delivered into biological cells in the penetrated tissues by an applied electric field. However, Hofmann is not applied alone, but in combination with Gross et al., which teaches this limitation, and the claimed invention becomes obvious when the references are considered together as a whole rather than each alone. Additionally, as pointed out above, Gross et al. does not teach away from any penetration into the skin and may be combined with Hofmann. Thus, the rejections are properly maintained.

Claims 25, 26, 29-31, 37, 47, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Meserol (US Pat. 6,090,617).

As discussed above, Gross et al. anticipates claims 25, 26, 29-30, 37, 47, 49, and 50. However, Gross et al. does not expressly disclose an electrode comprising a fixed electrode surface which is coated with a static layer of releasable molecules.

Meserol discloses electrodes coated with a metal nitride coating for use in a saline solution. See abstract.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the metal nitride coated electrodes disclosed in Meserol for use in the Gross drug delivery device. One of ordinary skill in the art would have been motivated to do this because Meserol points out that metal nitride coatings "protect surgical implants or instruments used in a biological system from corrosion and wearing due to externally generated forces, such as salts or friction" (column 1, lines 46-49). Meserol provides an improved metal nitride coated electrode which addresses problems concerning electric signal generation or stimulation in biological systems as described in column 1, lines 54-59. Moreover, the electrodes disclosed in Meserol "have substantially longer useful lives than conventional electrodes, due to their increased resistance to erosion and pitting normally caused by electrical signals emanating therefrom" (column 8, lines 54-57). Thus these coated electrodes would be desirable for use in practicing the Gross invention, where the electrodes are used for drug delivery in biological solutions or tissues. A holding of obviousness is clearly required.

Applicant's arguments have been fully considered but they are not persuasive. First, Applicant asserts that Meserol is irrelevant to the claimed invention since the coating disclosed in Meserol is not releasable and is not biologically active. However, the metal nitride coating disclosed in Meserol serves as the "fixed electrode surface" which, when combined with Gross et al., is coated with the Gross gel coating which is releasable and biologically active. Though the Gross electrode is protected by the gel coating, an metal nitride coating beneath it would offer additional protection. Combined with Gross et al., the metal nitride coating is not meant to substitute the gel coating. Thus, the rejections are properly maintained.

Claims 25, 26, 29, 30, 37, 38, 40, 42, 47, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Zewert et al. (US Pat. 5,749,847) and/or Widera et al. (Journal of Immunology, 2000, 164: 4635-4640).

As discussed above, Gross et al. anticipates claims 25, 26, 29, 30, 37, 47, 49, and 50. However, Gross et al. does not expressly disclose the delivery of vaccines, including polynucleotide, DNA, and RNA vaccines.

Zewert et al. teaches the use of electroporation for the delivery of nucleotides into an organism (column 2, lines10-14). More specifically, a composition comprising the nucleotide(s) is applied to the skin, and the skin is subsequently electroporated. The composition applied to the epidermis for drug delivery may include a vaccine (column 4, lines 32-34), and appropriate nucleotides for delivery include polynucleotides, deoxyribonucleotides (column 3, lines 44-46), and ribonucleic acid (column 4, lines 44-46).

Widera et al. discloses DNA vaccine delivery facilitated by electroporation (abstract). Needle array electrodes were used for electroporation following the injection of DNA or a DNA vaccine (page 4636, first column, "DNA immunization and in vivo electroporation").

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use polynucleotide, DNA, and RNA vaccines as drugs to be delivered when practicing the Gross invention. One of ordinary skill in the art would have been motivated to do this because the Gross invention involves electroporation for drug delivery, offering a device which accomplishes in a single step the methods of Zewert et al. and procedures performed in Widera et al. Moreover, Widera et al. concludes that "in vivo electroporation substantially increases DNA delivery and DNA vaccine potency, appears to be well tolerated by the animals, and is a simple technique that takes only a few seconds after inoculation" (page 4640, second paragraph). A holding of obviousness is clearly required.

Applicant's arguments have been fully considered but they are not persuasive. With respect to the Zewert reference, the Applicant asserts that the non-penetrating electrodes of Zewert et al. do not cause the nucleotide component to be delivered into the cells of the organism. However, Zewert et al. indicates that the invention can be used for electroporating tissue, "whereby at least a portion of the composition **enters** or passes across the tissue, thereby delivering the nucleotide into the tissue" (column 4, lines 52-55, emphasis added). Thus, nucleotides are delivered into tissue cells. Moreover, claim 1 recites that the stratum corneum is electroporated, and "at least a portion of the composition **enters** or passes across the stratum corneum, thereby delivering the nucleotide component into the organism" (emphasis added). In this case, nucleotides are delivered into the dead cells of the stratum corneum.

Further still, Applicant notes that the electrodes employed in Zewert et al. do not penetrate into tissues, and thus do not meet the limitations of the claimed invention of an electrode which penetrates into tissues and delivers molecules into biological cells in the penetrated tissues. It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. There is nothing in Zewert et al. that prevents the electrodes used in practicing the Zewert invention from being inserted into the skin, through the stratum corneum. Moreover, Zewert et al. is combined in an obviousness rejection with Gross et al., which also does not teach away from any penetration of electrodes into tissues.

With respect to the Widera reference, the Applicant argues that Widera et al. requires three apparatuses in contrast to the two required by the instant application, wherein a coated electrode is used. However, it is respectfully pointed out that Widera et al. is used in combination with Gross et al. which teaches a coated electrode. Thus, the rejections are properly maintained.

Claims 25, 26, 29, 30, 37, 44, 47, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Lerner (WO 97/18855).

As discussed above, Gross et al. anticipates claims 25, 26, 29, 30, 37, 47, 49, and 50. Gross et al. does not expressly disclose the delivery of protein-based vaccines.

Lerner discloses a drug delivery device comprising electrodes supporting a "drug or other biologically active substance or compound" (claim 9). Furthermore, drugs or other biologically active substances for delivery include bacterial vaccines (page 28, line 7), proteins (page 28, line 19), and viral vaccines (page 28, line 22).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to deliver protein-based vaccines when practicing the Gross invention. One of ordinary skill in the art would have been motivated to do this because Lerner teaches that a variety of drugs can be delivered when using electrodes. It would have been desirable to deliver protein-based drugs for vaccination of bacterial and viral diseases. A holding of obviousness is clearly required.

Applicant's arguments have been fully considered but they are not persuasive. Applicant asserts that Lerner does not teach the delivery of material into cells using electroporation. However, delivery of material occurs when practicing the Lerner invention, since in one embodiment, the active compound delivered passes the blood brain barrier (page33, lines 10-12). Clearly the active compound have to have been delivered into and out of cells of the blood brain barrier. Finally, it is noted that Lerner is combined with Gross et al., and the claimed invention becomes obvious when the references are considered together as a whole rather than each alone. Thus, the rejections are properly maintained.

Claims 25, 26, 29, 30, 37, 47, 49, 50, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al. in view of Weidlich et al. (US 5,103,837).

As discussed above, Gross et al. anticipates claims 25, 26, 29, 30, 37, 47, 49, and 50. Gross et al. does not expressly an electrode which includes a coating having at least one static layer of **solvent releasable molecules** to be delivered into biological cells in the penetrated tissues by an applied electric field.

Weidlich et al. discloses an implantable stimulating electrode which has a thin coating of a hydrophilic polymer containing an anti-inflammatory steroid which diffuses into surrounding tissue after implantation. Because the steroid can diffuse from the polymer, the anti-inflammatory steroid is a solvent releasable molecule to be delivered into biological cells.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have substituted the gel layer in the Gross electrode with the hydrophilic polymer with steroid as disclosed in Weidlich et al. One of ordinary skill in the art would have been motivated to make this substitution since there would have been improved delivery of the releasable molecules. There would have been improved delivery of the releasable molecules, which are the steroid molecules, since the molecules are simulataneously exported by diffusion and the electric field. Thus, a holding of obviousness is clearly required.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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